

CLAIMS

1. A method to detect analyte in an aqueous solution with use of agglutination reaction of polymer-based fine particles dispersed in said solution, which is characterized by:

(a) said fine particle has, as a core, a polymer chain segment with a chargeable group-carrying recurring unit, and has, as plural brushes on said core or as a shell, nonionic hydrophilic polymer chain or segment of said hydrophilic polymer chain, a residue of a member of a biologically specific bond which forms a counterpart to analyte being bound to at least a part of free terminals of said hydrophilic polymer chain,

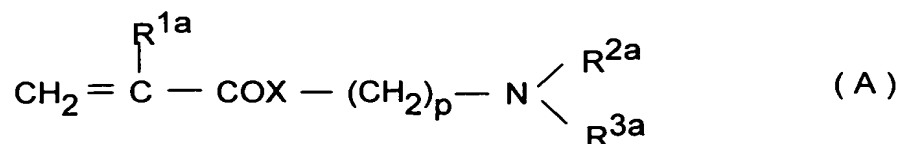
(b) agglutination reaction is conducted under a condition under which fine particles whose chargeable group is in a charged state can agglutinate via analyte, and, subsequently, thus agglutinated matter is treated under a condition under which, although the biologically specific bond between fine particles is not cleaved, the bond made by electrostatic interaction can be cleaved, and

(c) the existence of agglutinated matter which remains after the treatment of step (b) is used as an index of the presence of analyte.

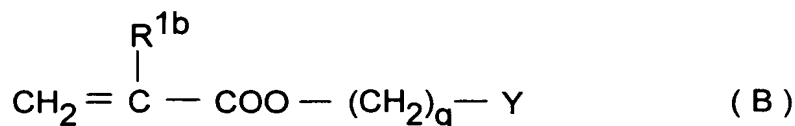
2. A method of claim 1 wherein the chargeable group in polymer-based fine particles is selected from the group consisting of tertiary amino group, secondary amino group, carboxyl group, sulfo group and phosphono group.

3. A method of claim 1 wherein the nonionic hydrophilic polymer chain in polymer-based fine particles is originated in polymer which is selected from the group consisting of polyethylene glycol, poly(vinyl alcohol), poly(vinyl pyrrolidone) and poly(N,N-dimethylacrylamide), and wherein the polymer chain carrying a chargeable group in the polymer-based fine particles is either composed of monomer having a

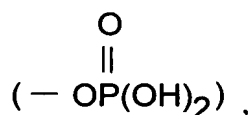
general formula (A):



wherein R^{1a} denotes a hydrogen atom or a C_{1-6} alkyl group, R^{2a} and R^{3a} either, independently, denote a C_{1-6} alkyl group or, taken together, may form, with the nitrogen atom to which they are bound, a five- or six-membered heterocycle which may contain further one or two nitrogen atoms, an oxygen atom or a sulfur atom, X denotes $-\text{O}-$ or $-\text{NH}-$, and p denotes an integer of 2 to 6;
or composed of monomer having a general formula (B):



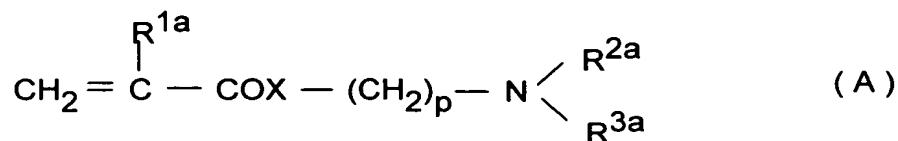
wherein R^{1b} denotes a hydrogen atom or a C_{1-6} alkyl group, Y denotes carboxyl group ($-\text{COOH}$), sulfo group ($-\text{SO}_3\text{H}$), oxysulfo group ($-\text{OSO}_3\text{H}$) or oxyphosphono group



q denotes an integer of 0 to 4, provided that, when q is 0, Y denotes a hydrogen atom;

or composed of a polymer selected from the group consisting of poly(lysine), poly(3- ω -N,N-di C_{1-6} alkylamino- C_{2-4} alkyl aspartate), poly(4- ω -N,N-di C_{1-6} alkylamino- C_{2-4} alkyl glutamate), poly(aspartic acid) and poly(glutamic acid).

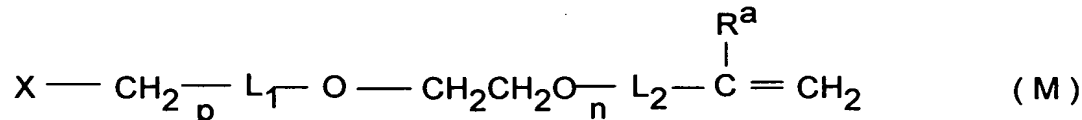
4. A method of claim 1 wherein the hydrophilic polymer chain in polymer-based fine particles is originated in polyethylene glycol, and wherein the polymer chain with a recurring unit carrying a chargeable group is composed of monomer having a general formula (A):



wherein R^{1a} denotes a hydrogen atom or a C_{1-6} alkyl group, R^{2a} and R^{3a} either, independently, denote a C_{1-6} alkyl group or, taken together, may form, with the nitrogen atom to which they are bound, a five- or six-membered heterocycle which may contain further one or two nitrogen atoms, an oxygen atom or a sulfur atom, X denotes $-O-$ or $-NH-$, and p denotes an integer of 2 to 6.

5. A method of claim 4 wherein the hydrophilic polymer chain segment and the polymer chain segment with a recurring unit carrying a chargeable group in polymer-based fine particles constitute a block copolymer.

6. A method of claim 4 wherein the hydrophilic polymer chain in polymer-based fine particles is formed from poly(ethylene glycol) macro monomer having formula (M):



wherein X denotes a hydrogen atom, $-COOM$ group (M denotes a hydrogen atom or an organic group), $-CHR^1R^2$ (R^1 and R^2 either independently denote a C_{1-6} alkyloxy group, phenyloxy group or a phenyl- C_{1-3} alkyloxy group, or, taken together, denote $-OCHR'-CH_2O-$ wherein R' denotes a hydrogen atom or a C_{1-6} alkyl group) or $-CH=O$,

R^a denotes a hydrogen atom or a C_{1-6} alkyl group,

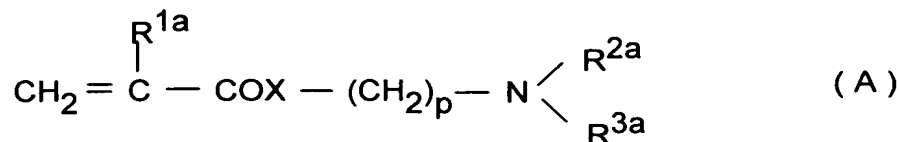
L_1 denotes a methylene group or a carbonyl group,

L_2 denotes a carbonyl group, a C_{1-3} alkylene group or a C_{1-3} alkylphenylene group,

n denotes an integer of 2 to 10,000, and

p denotes an integer of 1 to 5;

and wherein the polymer chain with a recurring unit carrying a chargeable group in polymer-based fine particles is formed from monomer having a general formula (A):



wherein R^{1a} denotes a hydrogen atom or a C_{1-6} alkyl group, R^{2a} and R^{3a} either, independently, denote a C_{1-6} alkyl group or, taken together, may form, with the nitrogen atom to which they are bound, a five- or six-membered heterocycle which may contain further one or two nitrogen atoms, an oxygen atom or a sulfur atom, X denotes $-\text{O}-$ or $-\text{NH}-$, and p denotes an integer of 2 to 6;
and wherein said two monomers are copolymerized with a crosslinking agent and/or an ethylenically polymerizable group-containing diluting monomer to give a random copolymer, said crosslinking agent and diluting monomer being allowed, where necessary, to be mixed with each other before crosslinked.

7. A method of anyone of claims 1 to 6 wherein the polymer-based fine particles have, encapsulated in their core domain, an ultrafine particle of inorganic material which is selected from the group consisting of semiconductor, free electron metal, magnetic material and silica.

8. A method of claim 4 wherein the polymer-based fine particles have, encapsulated in their core domain, an ultrafine particle of semiconductor.

9. A method of anyone of claims 1 to 8 wherein a residue of one of companion pieces of biologically specific bond is a residue of one of antibody and its antigen or hapten; a residue of one of receptor protein and lectin, hormone and neurotransmitter which are to bond the receptor protein; a residue of one of streptavidin and biotin derivative; and a residue of one of enzyme and its substrate.

10. A method of anyone of claims 1 to 7 wherein the condition under which, although the biologically specific bond is not cleaved, the bond

made by electrostatic interaction can be cleaved, is putting the agglutinated matter under a high concentration of salt.